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Clinical practice of respiratory virus diagnostics in critically ill patients with a suspected pneumonia: A prospective observational study

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ABSTRACT

Background: Clinical guidelines suggest testing for respiratory viruses during the influenza season, but are unclear which categories of patients on the intensive care unit (ICU) should be tested.
Objective: We described the clinical practice of diagnostic testing for respiratory virus infections in patients presenting to ICU with suspected community-acquired pneumonia (CAP) or hospital-acquired pneumonia (HAP).
Study design: Prospective observational study in consecutive CAP and HAP patients with an ICU stay of more than 24 h in two tertiary care hospitals in The Netherlands, from 2011 to December 2013. The proportion of patients receiving diagnostic testing with PCR for the presence of respiratory viruses in respiratory tract specimens was determined.
Results: In total, 1452 patients were included, of which 712 patients presented with CAP and 740 with HAP. In CAP, 282 of 712 (40%) were tested for respiratory viruses (190 of 417 (46%) during the influenza season). In HAP, 95 of 740 (13%) were tested (50 of 372 (13%) during the influenza season). Regardless of the season, virus diagnostic tests were ordered significantly more often in patients with comorbidities, and in those presenting with elevated CRP and leucopenia. In patients who were tested during the influenza season, the prevalence of influenza was 14% in patients with CAP and 10% in those with HAP. Influenza was absent during the summer in both groups.
Conclusions: Less than half of patients admitted to the ICU with suspected pneumonia were tested for the presence of viral pathogens, either in or outside the influenza season.

1. Background

Respiratory virus infections are important causes of community-acquired pneumonia (CAP) and respiratory failure both in children and adults [1]. Epidemiological studies show that the prevalence of viral respiratory tract infections can be as high as 41% in critically ill patients admitted to the intensive care unit (ICU) with a suspected CAP, and up to 34% in hospital-acquired pneumonia (HAP) [2–6]. Detection of such infections in critically ill patients may have important implications for infection control measures such as isolation and, in case of (suspected) influenza, rapid initiation of antiviral medication [7,8]. These measures have an impact on ICU resource use, mandating clear assessment of patients at risk of a viral respiratory tract infection.

A recent large retrospective study indicated that influenza infections are underdiagnosed in the critically ill [9]. However, current international clinical guidelines on virus diagnostics are not clear

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about which patients should receive testing in the ICU setting. The Infectious Diseases Society of America/American Thoracic Society (IDSA/ATS) consensus guidelines, as well as the International Guidelines for Management of Severe Sepsis and the European Respiratory Society/European Society for Clinical Microbiology and Infectious Diseases guidelines, state that testing for at least influenza should be considered in adult patients admitted with suspected respiratory infection during local epidemics [10–12], but all are unclear if all patients admitted to the ICU with a suspected CAP should be tested for respiratory viruses. There are no recommendations for virus testing in patients admitted to the ICU due to HAP. The current practice of testing for the presence of viral pathogens in critically ill patients with a suspected CAP or HAP is unknown.

2. Objectives

The practice of diagnostic testing for viral respiratory infections was described in patients admitted to the ICU with clinical symptoms suggestive for CAP or HAP. Also, the prevalence of virus infections as detected during routine care was reported.

3. Study design

3.1. Study population

This study is part of a multi-center prospective cohort study, in which consecutive patients admitted to the mixed ICUs of two tertiary care hospitals in The Netherlands were enrolled between January 1st 2011 and December 31st 2013 (clinicaltrials.gov Identifier: NCT01905033). For this study patients with suspected CAP or HAP were included. Exclusion criteria were admissions with a length of ICU stay of < 24 h and transfers from another ICU. The Ethics Committees of both participating centers approved an opt-out method of consent (protocol number 10-056C).

3.2. Study definitions

A suspected respiratory tract infection at ICU admission was defined by empiric or targeted use of systemic antibiotics for a suspected CAP or HAP initiated by the attending physicians, between seven days prior to, and two days after ICU admission. The most likely source of each infection was determined by assessment of clinical data, radiological imaging and culture results as ordered by routine care, using strict diagnostic criteria. These criteria were based on CDC criteria as well as the International Sepsis Forum Consensus Conference definitions for CAP and HAP, which were adapted to the Dutch situation as described previously [13]. All observers were trained in these definitions before the start of the study, and an electronic algorithm was used that alarmed the researchers when there were inconsistencies with other recorded clinical variables.

Respiratory virus diagnostics were defined as in-house polymerase chain reaction (PCR) tests ordered as per discretion of attending physicians on samples from the respiratory tract, either simplex or multiplex [14,15], for any of the following viruses: influenza virus A and B, respiratory syncytial virus, human metapneumovirus, parainfluenza virus 1–4, human rhinovirus, coronavirus, adenovirus, enterovirus, human bocavirus and parechovirus. Samples from the respiratory tract included nasopharyngeal swabs, throat swabs, bronchoalveolar lavage fluid, tracheobronchial aspirates, sputum and pleural puncture fluid.

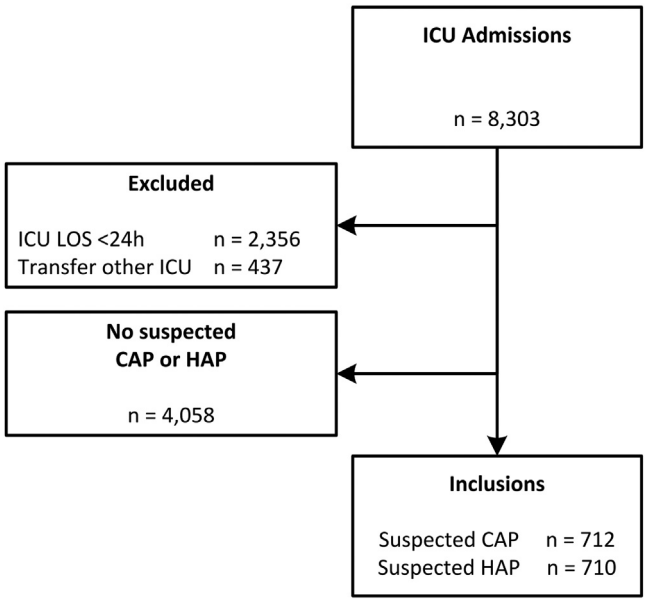

Fig. 1. Flowchart of patient inclusion.
Abbreviations: CAP = community-acquired pneumonia; HAP = hospital-acquired pneumonia; ICU = intensive care unit; LOS = length of stay.

3.3. Data analysis

The characteristics of patients who were tested were compared to patients not tested using non-parametric descriptive statistics. Numerical data was compared by Kruskal-Wallis tests, categorical data by Chi-square tests. Subgroup analyses were performed for the influenza season period and the period outside the season separately. Influenza season was defined between November 1st and April 30th. The prevalence of viral infections in those who were tested was reported. Treatment with oseltamivir was recorded, and the continuation, discontinuation or start of treatment was related to influenza test results. All analyses were performed using SAS 9.2 (Cary, NC, USA). P values less than 0.05 were considered to represent statistical differences.

4. Results

During the study period, a total of 8303 patients were admitted to the ICU, of whom 2356 were excluded because of an ICU stay of less than 24 h, 437 patients were transferred from another ICU, and 4058 did not have a suspected pneumonia. In total, 712 patients were included with a suspected CAP, and 740 patients with a suspected HAP (Fig. 1).

4.1. Proportion of patients tested for respiratory viruses

In the group of patients admitted to the ICU with a suspected CAP, 282 of 712 patients (40%) were tested for respiratory viruses; of patients admitted with a suspected HAP, 95 of 740 (13%) were tested (P = <0.001).

4.2. Characteristics of tested and non-tested patients with suspected CAP

Patients admitted with a suspected CAP who were tested, significantly more often had comorbidities (including chronic obstructive pulmonary disease (COPD), chronic renal insufficiency and immune deficiency) compared to those who were not tested (Table 1). Also, within 24 h of ICU admission, tested patients had a